UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/709,691	05/24/2004	Itzhak Bentwich	050992.0400.01USCP	3690

37808 7590 12/16/2009

ROSETTA-GENOMICS
c/o POLSINELLI SHUGHART PC
700 W. 47TH STREET
SUITE 1000
KANSAS CITY, MO 64112

EXAMINER	
WOLLENBERGER, LOUIS V	
ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
12/16/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/709,691	BENTWICH ET AL.	
	Examiner	Art Unit	
	Louis Wollenberger	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,25,31,33,39 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *25 and 33* is/are allowed.

6)☒ Claim(s) *23,31,39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/21/2009 has been entered.

Status of Application/Amendment/Claims

Applicant's response filed 10/21/2009 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 7/23/2009 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Applicant's amendments to the claims filed 10/21/2009 are acknowledged. With entry of the amendment, Claims 23, 25, 31, 33, 39, and 40 are pending and under consideration.

Specification

The application contains disclosure entirely outside the bounds of the allowed claims. Applicant is required to modify the brief summary of the invention and restrict the descriptive matter so as to be in harmony with the claims (MPEP § 1302.01).

In the instant case the specification incorporates by reference several large tables, Tables 1-11, submitted to the Office in the form of compact discs, which, altogether, are said by applicant to contain several thousand kilobytes of information, the large majority of which is not pertinent to the claimed invention: SEQ ID NO:348 and 4233864.

Using the conversion factor set forth in 37 CFR 1.52(f)(1), the electronic information contained in Tables 1-11 represents tens if not hundreds of thousands of sheets of additional disclosure beyond the approximately 162 pages of paper copy specification filed therewith. A review of Tables 1-11 finds the tables disclose information directed to hundreds of thousands of different nucleotide sequences that have no disclosed relation to the claimed sequences.

In addition to the requirement under MPEP 1302.01, Applicant is required under 37 CFR 1.52(e)(5) to amend the specification to include in the paper portion of the specification all descriptive matter pertinent to SEQ ID NO:348 and 4233864 that was previously submitted in tables on compact disc. Amendments to the specification must comply with 37 CFR 1.121 and 1.125.

Applicant's Reply

In the remarks filed 10/21/2009, Applicant states responsive amendments will be filed in a supplemental reply.

Claim Objections

Claim 39 is objected to because of an apparent typographical error: "acide" in line 3.

Claim Rejections - 35 USC § 112, first paragraph (written description)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Upon further consideration, Claims 23, 31, and 39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains

subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, complete or partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient.

Embodiments (c) and (d) of Independent Claim 23 expressly embrace all nucleic acid sequences 19-24 nucleotides in length that are at least 80% identical to the 22-nucleotide sequence of SEQ ID NO:348 as well as all 19-24-nucleltide complements thereof.

The specification teaches that SEQ ID NO:348 is a mature miRNA that is produced in the cell from a preprocessed hairpin RNA corresponding to SEQ ID NO:423864. Upon hybridization with the mRNA of the gene cysQ of *P. putida*, the mature miRNA is claimed to inhibit expression of the gene (Remarks filed 6/29/2009).

The specification teaches at Paragraphs 50, 54, and 216 that:

> [0050] A "Hairpin-Shaped Precursor" is defined as a Hairpin Structure which is processed by a Dicer enzyme complex, yielding an oligonucleotide which is about 19 to about 24 nts in length.

[0216] When initially assessing a novel GAM FOLDED PRECURSOR RNA, each 19-24 nt-long segment thereof is considered to be a potential GAM RNA, because the Dicer-cut location is initially unknown.

[0054] There is thus provided in accordance with a preferred embodiment of the present invention a bioinformatically detectable isolated oligonucleotide which is endogenously processed from a hairpin-shaped precursor, and anneals to a portion of a mRNA transcript of a target gene, wherein binding of the oligonucleotide to the mRNA transcript represses expression of the target gene, and wherein the oligonucleotide has at least 80% sequence identity with a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-385 and 386-49787.

Accordingly, while the bioinformatic prediction program used to identify potential precursor and processed miRNAs is programmed to search for potential 19-24 nucleotide fragments, there is no disclosure showing or suggesting that each particular mature miRNA actually identified by the program can perform the same function as an miRNA as any 19, 20, 23, or 24 nucleotide fragment thereof, much less any 19, 20, 21, 23, or 24 nucleotide fragment thereof that is only 80% identical to the actual predicted sequence, SEQ ID NO:348. With regard to SEQ ID NO:348, there is no disclosure showing which 1, 2, or 3 nucleotides can vary while

maintaining the asserted function, or any disclosure remotely describing which 20% of the nucleotides may vary while maintaining miRNA-like function, or any gene-specific utility. Indeed embodiment c of claim 23 is far broader than the supporting disclosure. For example, a 19-nt sequence that is only 80% identical to SEQ ID NO:348 includes a sequence that shares 16 nucleotides in common with SEQ ID NO:348. Given the particular, less-than-fully complementary mode by which an miRNA recognizes and binds its cognate mRNA target (See for example Table 7, cited in part at page 12 of the Remarks filed 6/29/2007, there is no disclosure or evidence showing that any 6 nucleotides of SEQ ID NO:348 may be removed while maintaining its disclosed utility, much less any disclosure showing which 6 nucleotides may be removed while maintaining its disclosed utility.

Though the specification provides literal antecedent basis for the claimed limitations, the mere words do not show possession of the claimed invention having the disclosed utility.

While the Application adequately describes and shows possession of the nucleotide sequences SEQ ID NO:348 and 4233864, the hairpin miRNA precursor from which SEQ ID NO:159 is said to derive, and indicates that such sequences will more likely than not inhibit the expression of a known gene, the application does not describe the genus of sequences defined by the claims that have this function or that have any other well established function. Thus, the claims are extremely broad. Adequate written description does not exist in the instant application for all these sequences. While Applicant has disclosed the relevant identifying features of SEQ ID NO:348 for performing the function disclosed in the specification, Applicant has not disclosed the identity all sequences of 19, 20, 21, 23, and 24 nucleotides in length that will perform this function. Applicant, for example, has not disclosed which 2-3 nucleotides may be

added or subtracted from the sequence while retaining the disclosed activity, nor is there any evidence to show that any 2-3 nucleotides may be added or subtracted while retaining the asserted utility. While the specification discloses that a hairpin precursor may be anywhere from 50-140 nucleotides in length and may be processed by a dicer enzyme to yield an oligonucleotide that is 19 to 24 nucleotides in length, these passages simply summarize the possible lengths of miRNAs in a cell and are not equivalent to disclosure that the miRNA corresponding to SEQ ID NO:348 or its precursor, SEQ ID NO:4233864, may be of any length in this range, and there is no evidence to show the activity associated with these sequences (i.e., structures) could be extrapolated to any and all nucleotide sequences having only 19 nucleotides of SEQ ID NO:348, much less only 15-16 nucleotides of SEQ ID NO:348. Applicant provides no disclosure showing which nucleotides or at what position nucleotides may be added or subtracted while retaining the activity specific to the invention. In fact the Examiner is unable to find any passage or evidence in the application as filed expressly or impliedly conveying that any consecutive 19-nucleotide sequence of SEQ ID NO:348 may be used to regulate cysQ expression or even to sequence-specifically probe for cysQ. Moreover, Applicant has not disclosed which sequences may be added and where to SEQ ID NO:348 while retaining its specific activity.

Certainly, the application does not disclose by words or any other representation that any 19-24 or 50-140 nucleotide sequence having a mere 73% (16 of 22 nts) identity to SEQ ID NO:348 is a part of the invention, as now claimed in part (c) of claims 23.

Accordingly, only those sequences consisting of, complementary to, and encoded by and equivalent in length to SEQ ID NO:348 and 4233864 are adequately described in the specification.

Applicant is reminded that the written description requirement is separate and distinct from the enablement requirement. *In re Barker*, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978); *Vas-Cath, Inc.* v. *Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991).

Claim Rejections - 35 USC § 102

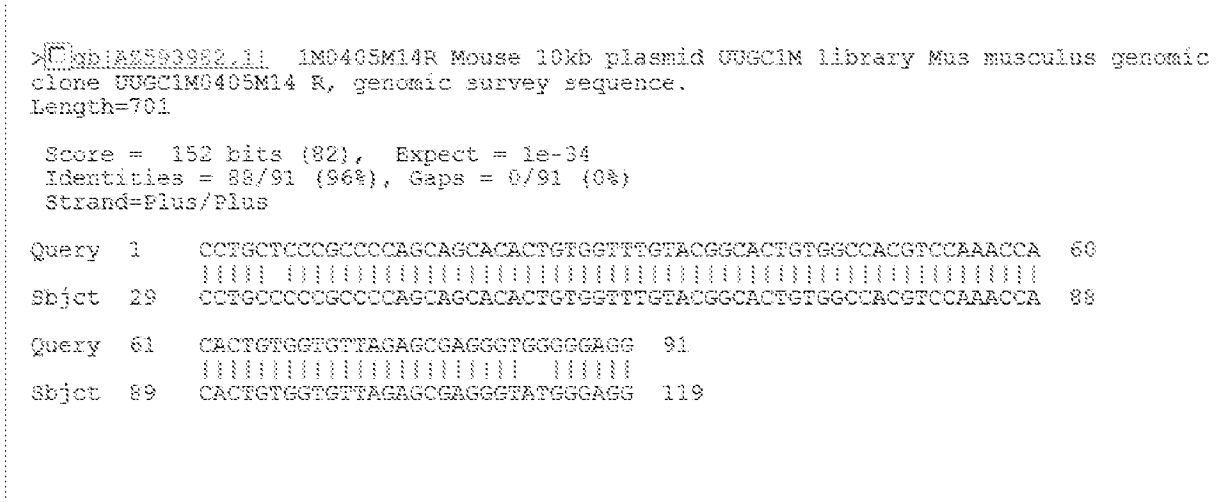
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 39 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Dunn et al. GenBank Accession No. AZ593982, published online at NCBI on December 13, 2000.

As shown by the alignment below, Dunn et al. taught a nucleic acid sequence comprising instant SEQ ID NO:348 and SEQ ID NO:4233864. The sequence disclosed by Dunn et al. is indistinguishable from the probes (i.e., nucleic acid) defined by claims 39 and 40. Claims 39 and 40 as written continue to use open "comprising" language. The claims do not clearly exclude other nucleic acid sequences flanking or contiguous with the human insert. The plain meaning of the term "insert" clearly implies the probe may contain one or more additional nucleotides on one or both sides of "the human insert" and there is no language excluding the additional one or more nucleotides from being human nucleotides. Referring to a nucleic acid sequence as an

"insert" in the context of a probe raises the reasonable presumption the sequence has been inserted into something such as another nucleic acid sequence. The term would be readily recognized in the art of molecular cloning, wherein sequences are inserted into larger sequences such as vectors, as by restriction and ligation.



```
>gb|AZ593982.1|  1M0405M14R Mouse 10kb plasmid UUGC1M library Mus musculus genomic
clone UUGC1M0405M14 R, genomic survey sequence.
Length=701

 Score =  152 bits (82),  Expect = 1e-34
 Identities = 88/91 (96%), Gaps = 0/91 (0%)
 Strand=Plus/Plus

Query  1    CCTGCTCCCGCCCCAGCAGCACACTGTGGTTTGTACGGCACTGTGGCCACGTCCAAACCA  60
            ||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  29   CCTGCCCCCGCCCCAGCAGCACACTGTGGTTTGTACGGCACTGTGGCCACGTCCAAACCA  88

Query  61   CACTGTGGGTGTTAGAGCGAGGGTGGGGGAGG  91
            ||||||||||||||||||||  |||||
Sbjct  89   CACTGTGGTGTTAGAGCGAGGGTATGGGAGG  119
```

***

Claims 39 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Birren et al., GenBank Acc. No. AC015918 "Homo sapiens chromosome 17 clone CTD-3165O8 map 17", published online by NCBI on March 27, 2003. (The reference contains a lengthy sequence disclosure. Applicant is provided with the first 3 pages disclosing features relevant to the rejection and a portion of the sequence

As shown by the alignment below, Birren et al. disclosed a human BAC clone (i.e., vector) comprising a nucleic acid sequence that comprises instant SEQ ID NO:348 and 4233864. The vector disclosed by Birren et al. is indistinguishable from the probes (i.e., nucleic acid) defined by claims 39 and 40 and would be capable of being used as a probe. Accordingly, Birren et al. anticipates the instant claims.

```
>gb|AC015918.10| Homo sapiens chromosome 17 clone CTD-3165O8 map 17, 21 unordered
pieces
Length=220581

 Score =  169 bits (91),  Expect = 2e-39
 Identities = 91/91 (100%), Gaps = 0/91 (0%)
 Strand=Plus/Minus

Query  1       CCTGCTCCCGCCCCAGCAGCACACTGTGGTTTGTACGGCACTGTGGCCACGTCCAAACCA  60
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  40348   CCTGCTCCCGCCCCAGCAGCACACTGTGGTTTGTACGGCACTGTGGCCACGTCCAAACCA  40289

Query  61      CACTGTGGTGTTAGAGCGAGGGTGGGGGAGG  91
               ||||||||||||||||||||||||||||||||
Sbjct  40288   CACTGTGGTGTTAGAGCGAGGGTGGGGGAGG  40258
```

****

Claims 23, 31, and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by Tuschl et al. (US Patent 7,232,806).

As shown by the alignment below, Tuschl et al. disclosed a 21 nucleotide sequence that has at least 17 nucleotides in common with instant SEQ ID NO:348. The sequence is therefore at least 80% identical to SEQ ID NO:348. Neither claim 23 nor the specification defines the method by which percent identity is to be calculated (relative to the length of SEQ ID NO:348 or the length of the 19-24 nt nucleic acid).

Vectors thereof and diagnostic/detection (i.e., probe) applications are also disclosed (col. 2 bridging to 3; and col. 11, line 9).

```
RESULT 8
US-10-490-955-19
; Sequence 19, Application US/10490955
; Patent No. 7232806
; GENERAL INFORMATION:
;  APPLICANT: Tuschl, Thomas
;  APPLICANT:  Lagos-Quintana, Mariana
;  APPLICANT:  Lendeckel, Winfried
;  APPLICANT:  Meyer, Jutta
;  APPLICANT:  Rauhut, Reinhard
;  TITLE OF INVENTION: MicroRNA Molecules
;  FILE REFERENCE: 2923-613
;  CURRENT APPLICATION NUMBER: US/10/490,955
;  CURRENT FILING DATE:  2004-03-29
;  PRIOR APPLICATION NUMBER: PCT/EP02/10881
;  PRIOR FILING DATE: 2002-09-27
;  PRIOR APPLICATION NUMBER: EP 02 016 772.2
;  PRIOR FILING DATE: 2002-07-26
;  PRIOR APPLICATION NUMBER: EP 02 006 712.0
;  PRIOR FILING DATE: 2002-03-22
```

```
;  PRIOR APPLICATION NUMBER: EP 01 123 453.1
;  PRIOR FILING DATE: 2001-09-28
;  NUMBER OF SEQ ID NOS: 562
;  SOFTWARE: PatentIn version 3.2
; SEQ ID NO 19
;   LENGTH: 21
;   TYPE: DNA
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Oligonucleotide probe with significant homology to D.
;   OTHER INFORMATION: melanogaster, HeLa cell, mouse kidney, adult zebrafish and frog
;   OTHER INFORMATION: ovary miR-15
US-10-490-955-19

  Query Match             69.1%;  Score 15.2;  DB 5;  Length 21;
  Best Local Similarity   60.0%;  Pred. No. 1.4e+03;
  Matches   12;  Conservative    5;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          2 AGCAGCACACUGUGGUUUGU 21
              |||||||||   :||:::|:
Db          2 AGCAGCACATAATGGTTTGT 21
```

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 23, 31, and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhou (US Patent 7,250,289).

Zhou disclosed and claims arrays comprising a plurality of 25-nucleotide nucleic acid probes. Methods for synthesizing (i.e., isolating) and using each probe in the array are disclosed. One probe, SEQ ID NO:669995, is at least 80% identical/complementary to instant SEQ ID NO:348 and its complements, as defined by claim 23, parts c and d (see alignment below). Zhou taught that nucleic acids of their invention may range from at least 2 to preferably at least 8, 15 or 20 nucleotides in length (col. 6 and elsewhere). At column 8, it is taught the nucleic acids spotted onto the array can be essentially of any length from 1 to 1000 monomers. Accordingly, one of skill would reasonably have envisioned nucleic acid probes of at least 8 to 25 nucleotides in length corresponding to any of the disclosed nucleic acid probes, including SEQ ID NO: 669995. One of skill would reasonably have been led to make and use any of these probes because Zhou states that any probe of any length, including those lengths specifically suggested, may be used on the array. One would reasonably expect the 24-mer or 23 mer equivalents of SEQ ID NO: 669995, or any other probed disclosed therein, to have substantially the same hybridization properties as SEQ ID NO: 669995, and would reasonably be motivated to make and use shorter nucleic acids for purposes of economy. 24-mer or even 23 mer equivalents of SEQ ID NO: 669995 necessarily include sequences at least 80% identical/complementary to instant SEQ ID NO:348, DNA encoding SEQ ID NO:348, and complements thereof. That is, trimming one nucleotide from either end of the 25-mer would not affect the percent identity to the instantly claimed nucleic acid. Accordingly, synthesizing an array according to Zhou et al. in which each probe was nucleotides in length would result in the production of a 24 nucleotide sequence identical to that now claimed in part c of claim 23. The 25-nucleotide sequence would also be indistinguishable from the probe defined by claim 39. It would further have been obvious

to make and use a recombinant vector comprising any of the disclosed nucleic acid fragments to have a reproducible source of the fragments. Zhou et al. disclosed vectors comprising such fragments at column 8, line 45.

Accordingly, in view of Zhou et al., one of skill would have been led to make and use a nucleic acid sequence identical to that now claimed with the reasonable expectation that sequence would be useful and suitable for the same purpose disclosed by Zhou et al.

```
RESULT 6
US-10-719-900-669995/c
; Sequence 669995, Application US/10719900
; Patent No. 7250289
; GENERAL INFORMATION:
;  APPLICANT: Xue Mei Zhou
;  TITLE OF INVENTION: Methods of Genetic Analysis of Mouse
;  FILE REFERENCE: 3528.1
;  CURRENT APPLICATION NUMBER: US/10/719,900
;  CURRENT FILING DATE:  2003-11-20
;  PRIOR APPLICATION NUMBER: 60/427,808
;  PRIOR FILING DATE: 2002 11 20
;  NUMBER OF SEQ ID NOS: 982914
;  SOFTWARE: Microarray Probe Sequence Listing Generator V 1.1
; Patent No. 7250289
; SEQ ID NO 669995
;   LENGTH: 25
;   TYPE: DNA
;   ORGANISM: Mus musculus
US-10-719-900-669995

  Query Match             70.9%;  Score 15.6;  DB 5;  Length 25;
  Best Local Similarity   68.2%;  Pred. No. 9.1e+02;
  Matches   15;  Conservative    3;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 CAGCAGCACACUGUGGUUUGUA 22
              |||||||||||  |:||  : :|
Db         23 CAGCAGCACACAGTGGACTCTA 2
```

Response to Arguments

In reply to the previous rejection of the claims over Zhou et al., Applicant argues Zhou et al. does not teach using any of the disclosed probes as miRNAs (microRNAs). For example, Applicant argues Zhou et al. does not teach using any of the probes to regulate target gene sequences *in trans*. This argument is not persuasive because the instant claims are not limited to any method of using the claimed nucleic acid. The claims are drawn to a composition of matter, a nucleic acid, not methods of using the nucleic acid. Any reference in the prior art disclosing the nucleic acid or reasonably leading one of skill to make the nucleic acid for any purpose is

relevant to the question of anticipation or obviousness of a claimed nucleic acid. For purposes of the instant rejection of the instant nucleic acid as being obvious, it is not necessary for Zhou et al. to have disclosed or even recognized a use for the nucleic acid identical or similar to Applicant's intended use (MPEP 2144). The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. See, e.g., *In re Kahn*, 441 F.3d 977, 987, 78 USPQ2d 1329, 1336. One of skill would reasonably have understood and appreciated that each of the 25-nt probes disclosed by Zhou et al. could be synthesized as an 8-25 nucleotide sequence, including, for example, a 24-nt sequence, and used for the same purpose: array-based detection of a particular mRNA sequence.

Applicant also argues the massive number of sequences disclosed by Zhou et al. prevents one of skill from envisioning the claimed subgenus. However, there is no need here to envision any one sequence apart from any other. Zhou et al. is a US Patent, disclosing and claiming arrays comprising SEQ ID Nos.1-982,914. See claims 1-6. The patented arrays, therefore, include SEQ ID NO: 669995. Thus, each array and each probe on the array are described in the manner required by 35 USC 112, first paragraph. One of skill might reasonably infer, based on the supporting disclosure, that all of the nucleic acid probes recited for use on the claimed arrays may be synthesized and used in the form of an at least 8 to 25 nucleotide sequence for the detection/diagnostic purposed described therein, based on the supporting disclosure in Zhou et al. The set of arrays comprising, for example, all 24-nt probes produced from SEQ ID Nos.1-982,914 disclosed by Zhou et al. would necessarily include an array having a 24-nucleloide

version of SEQ ID NO:669995 that is 80% identical to the claimed nucleic acid sequence. One of skill might reasonably trim one nucleotide from either the 5' or 3' end of each probe, including SEQ ID NO:669995, to save on the costs of synthesizing and printing the array, with the reasonable expectation, in view of the disclosure in Zhou et al. that 8-25 nucleotide probes are suitable, these arrays would function in substantially the same manner for the same purpose.

***

Claims 23, 31, and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tuschl et al. (US Patent 7,232,806).

As shown by the alignment below, Tuschl et al. disclosed at Table 2 a mature, 22-nucleotide miRNA, miR-15, that has 17 nucleotides in common with instant SEQ ID NO:348. Tuschl et al. further assert their invention relates to any nucleic acid molecule that is the complement any sequence shown in Table 2, or that is at least 80% identical to any sequence in Table 2, or that hybridizes under stringent conditions to any such sequence (col. 1). Tuschl et al. also state that mature miRNAs usually have a length of 19-24 nucleotides, particularly 21, 22, or 23 nucleotides (col. 2).

Vectors thereof and diagnostic/detection (i.e., probe) applications for any of the disclosed miRNAs are also disclosed (col. 2 bridging to 3; and col. 11, line 9).

Accordingly, the set of 19-24 nucleic acid molecules having at least 80% identity to the miRNA disclosed therein as SEQ ID NO:81 reasonably overlap in scope with those defined by embodiments (c) and (d) of instant claim 23. The public was, therefore, reasonably in possession of sequences within the scope of the instant claims prior to the date of invention. It would have been obvious to make and use any of the disclosed sequences for the purposes disclosed therein

(regulation of gene expression or detection of miRNAs) since Tuschl et al. taught that any of the sequences may be used for any of these purposes.

```
RESULT 11
US-10-490-955-81
; Sequence 81, Application US/10490955
; Patent No. 7232806
; GENERAL INFORMATION:
;  APPLICANT: Tuschl, Thomas
;  APPLICANT:  Lagos-Quintana, Mariana
;  APPLICANT:  Lendeckel, Winfried
;  APPLICANT:  Meyer, Jutta
;  APPLICANT:  Rauhut, Reinhard
;  TITLE OF INVENTION: MicroRNA Molecules
;  FILE REFERENCE: 2923-613
;  CURRENT APPLICATION NUMBER: US/10/490,955
;  CURRENT FILING DATE:  2004-03-29
;  PRIOR APPLICATION NUMBER: PCT/EP02/10881
;  PRIOR FILING DATE: 2002-09-27
;  PRIOR APPLICATION NUMBER: EP 02 016 772.2
;  PRIOR FILING DATE: 2002-07-26
;  PRIOR APPLICATION NUMBER: EP 02 006 712.0
;  PRIOR FILING DATE: 2002-03-22
;  PRIOR APPLICATION NUMBER: EP 01 123 453.1
;  PRIOR FILING DATE: 2001-09-28
;  NUMBER OF SEQ ID NOS: 562
;  SOFTWARE: PatentIn version 3.2
; SEQ ID NO 81
;   LENGTH: 22
;   TYPE: RNA
;   ORGANISM: Homo sapiens
US-10-490-955-81

  Query Match             69.1%;  Score 15.2;  DB 5;  Length 22;
  Best Local Similarity   85.0%;  Pred. No. 1.4e+03;
  Matches   17;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          2 AGCAGCACACUGUGGUUUGU 21
              |||||||||   ||||||||
Db          2 AGCAGCACAUAAUGGUUUGU 21
```

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis Wollenberger whose telephone number is (571)272-8144. The examiner can normally be reached on M-F, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tracy Vivlemore can be reached on (571)272-2914. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Louis Wollenberger/
Primary Examiner, Art Unit 1635
December 12, 2009